REMARKS

In the present Amendment, claims 37, 53, 68, 70, 78, 87 and 92 have been amended to delete "a mustard oil" therein. Claims 1-36 and 55-63 were previously canceled. No new matter has been added.

Applicants respectfully submit that entry of the amendments, after final, is proper, at least because they place the application either in condition for allowance or in better form for appeal. See M.P.E.P. § 714.12. Upon entry of the Amendment, claims 37-54 and 64-95 will be all the claims pending in the application.

I. Response to Rejections under 35 U.S.C. § 103(a)

a. Claims 37, 38, 41-44, 47-54, 68-80 and 82-95 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Robinson et al., *Contact Dermatitis*, "Evaluation of a quantitative clinical method for assessment of sensory skin irritation," 45:205-213, 2001.

b. Claim 81 was rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Robinson et al., and further in view of Seidenari et al., *Contact Dermatitis*, 1998; 38(6):311-315, abstract only.

Applicants respectfully traverse the rejections for the reasons of record and the following additional reasons.

Independent claims 37 and 53 recite a non-therapeutic method of identifying persons having sensitive skin to a capsaicinoid, comprising, *inter alia,* applying to a skin area of an adult individual an aqueous or aqueous-alcoholic solution, comprising a stimulant that is a capsaicinoid at a concentration of between $1 \times 10^{-6}\%$ and $5 \times 10^{-4}\%$.

In addition, independent claims 68, 70, 78, 87 and 92 are directed to a method of evaluating the level of skin neurosensitivity of an adult individual to a capsaicinoid, comprising, *inter alia*, applying to a skin area of the individual a composition comprising a

physiologically acceptable vehicle that is an aqueous or aqueous-alcoholic solution and a peripheral nervous system stimulant that is a capsaicinoid, the concentration of the stimulant being between $1 \times 10^{-6}\%$ and $5 \times 10^{-4}\%$ (or $1 \times 10^{-4}\%$) by weight relative to the total weight of the composition.

One objective of the present invention is to further increase the diversity of models and devices available to the public for evaluating the skin sensitivity of an individual and provide a test allowing the determination of a sensitive skin population. Having sensitive skin is a permanent state characterized by sensitivity of skin to very low concentrations , such as $1 \times 10^{-6}\%$ and $5 \times 10^{-4}\%$ by weight, of a peripheral nervous system stimulant. Applicants advise that the studies regarding sensitive skin have shown that the threshold of sensitivity of the skin was very low, e.g., less than 1.10 - 3%.

The present specification demonstrates the importance of the presently recited concentrations of peripheral nervous system stimulant in evaluating the level of skin neurosensitivity. For example, as described in paragraph [0116] of the present specification, the subjects who detected $3.16 \times 10^{-5}\%$ (C1), $1 \times 10^{-4}\%$ (C2) and $3.16 \times 10^{-4}\%$ (C3) form a "sensitive to highly sensitive" population, and the subjects who detected $1 \times 10^{-3}\%$ (C4) and $3.16 \times 10^{-3}\%$ (C5) and who did not detect any concentration form a "virtually or completely insensitive" population (see, also, Fig. 6; paragraph [0101]). Therefore, using a concentration of $1 \times 10^{-3}\%$ or higher would not allow the determination of a sensitive skin population or the evaluation of the level of skin neurosensitivity.

In addition, the recited concentration of the peripheral nervous system stimulant is critical because when using more concentrated solutions, the test may lead to false positive results. For example, when subjected to a test using a peripheral nervous system stimulant

with a higher concentration, an individual who does not have sensitive skin may be caused to feel unpleasant sensation, thereby leading to false positive results.

Furthermore, as described in an article entitled "Detection Thresholds of Capsaicin: A New Test to Assess Facial Skin Neurosensitivity," by Roland JOURDAIN et al. J. Cosmet. Sci., 56, 153-156 (May/June 2005), which is partially authored by the present inventors and a copy of which has previously been submitted on September 28, 2007, using relatively low concentrations of capsaicine, such as those defined in the present claims, can allow the detection of sensitivity, which is not dependent upon subject's appreciation (relevant to claims 68, 70, 78, 87 and 92).

Moreover, the use of low concentrations of peripheral nervous system stimulant, such as capsaicine, as recited in the present claims, allows use of a lower concentration of physiologically acceptable vehicle, such as ethanol. As such, the test can be applied on the face of an individual.

Robinson et al. aims to the development of "better methods for predictive testing and risk assessment" of dermatological products and standard tests for the evaluation of irritant potential of new topical ingredients or products. It is clear throughout the article that individual subjects were tested regardless the sensitivity of their skin. The purpose of Robinson et al. is to characterize a product and not a population of subjects. Robinson et al. concludes that the "use of recall/imagined skin sensation perception data for prediction of actual reactivity to chemical probes may have screening utility depending on the survey questions used" (see, Abstract).

Particularly, Robinson et al. describes studies related to response of individual subjects to a topical application of chemosensory irritant chemicals using the labeled

magnitude (LM) scale, for pre-market dermatotoxicologic safety testing and risk assessment (page 211, paragraph bridging left and right column).

The capsaicin treatment studies in Robinson et al. were performed by using capsaicin in 80% ethanol at concentrations of 100 to 10,000 mM (page 206, right column, first paragraph), which correspond to 3.12×10^{-3}% to 3.12×10^{-1}% by weight and thus fall outside the ranges recited in present claims 37, 53, 68, 70, 78, 87 and 92. In addition, Robinson et al. does not disclose or suggest the above noted unexpected results achievable by using capsaicin solutions with concentrations between 1×10^{-6}% and 5×10^{-4}% by weight.

Further, Robinson et al. describes in one part of the study, intensities of self-assessed sensations and of experimental application of chemicals are compared. Specifically, the study procedure consists of (i) questioning subjects on the intensity of recalled/imagined sensations when testing these subjects with a product; and then (ii) identifying the degree of correlation between self-perceived reactivity to recall/imagined skin stimuli and actual measured chemosensory responses.

Robinson et al. further states that "the results of the capsaicin study showed some degree of correlation between self-perceived 'reactivity' to recall/imagined skin stimuli and actual measured chemosensory responses" (page 210, right column, third paragraph; page 212, right column, first paragraph). However, the conclusion of this part of the study is that no consistency exists between the intensity of the recalled/imagined sensations and the actual measured chemosensory reactivity after applying a product (see page 210 and Fig. 7). That is, there is no clear pattern of answers or correlation between these answers and cutaneous reaction of tested individuals.

Concerning another part of the study in Robinson et al., considerable variability between individual subjects was found when testing with capsaicine, even across the range of skin sensations described.

In view of the descriptions in Robinson et al. as a whole, one of ordinary skill in the art would rather have been taught away from using capsaicine to elaborate a method to classify one population, e.g., concerned with sensitive skin. Indeed, variability between individual subjects has to be avoided to achieve a reliable method to evaluate the level of skin neurosensitivity.

The Office Action alleges that "one of ordinary skill in the art would understand the general principles of optimizing the concentrations of neurostimulants and diluents such as for pharmacological testing" (page 6, last paragraph of the Office Action).

However, the Office Action has failed to point to any evidence showing that application of capsaicin solutions at concentrations lower than 100 mM in Robinson et al.'s study would provide predictable results in providing the desired information.

Moreover, as noted above, Robinson et al. does not address the issue of sensitive skin, as described in the present application. Furthermore, Robinson et al. does not correlate high reactivity to a peripheral nervous system stimulant to sensitive skin. Thus, it would not have been obvious to a skilled artisan to try to vary a peripheral nervous system stimulant dose allowing the identification of sensitive skin, and particularly, to reduce the stimulant dose to identify a person with sensitive skin.

Similarly, the Office Action has not established that modifying Robinson et al. by replacing 80% ethanol with ethanol having concentration different from 80%, e.g., 1% to 50%, 5% to 20%, 8% to 15%, and 10%, as recited in present claims 48-51, 77 and 82-85, would provide predictable results in providing the desired information.

Seidenari et al. is cited for the disclosure of a sting test including applying an irritant to the nasolabial fold. As Seidenari et al. does not rectify the above noted deficiencies of Robinson et al., the combination of Seidenari et al. and Robinson et al. still would not result in the subject matter of present claims 37, 53, 68, 70, 78, 87 and 92.

In view of the foregoing, Applicants respectfully submit that claims 37, 53, 68, 70, 78, 87 and 92 are patentable over Robinson et al., alone or in combination with Seidenari et al., and thus the rejections should be withdrawn. Additionally, claims 38, 41-44, 47-52, 54, 69, 71-77, 79-86, 88-91 and 93-95 depend from claim 37, 53, 68, 70, 78, 87 or 92, and thus are patentable over the cited references at least by virtue of their dependency and the above additional reasons.

II. Response to Rejection under 35 U.S.C. § 112

Claims 37, 38, 41-44, 47-54 and 68-95 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants respectfully submit that the claims as amended are not indefinite.

Specifically, independent claims 37, 53, 68, 70, 78, 87 and 92 have been amended to delete "a mustard oil" therein. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection.

III. Conclusion

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is earnestly solicited. If there are any

questions concerning this paper or the application in general, the Examiner is invited to telephone the undersigned at her earliest convenience.

Respectfully submitted,

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